Effect of Rutin on Increased Capillary Fragility in Man.

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Rutin is, like hesperidin, a flavone glucoside, and the two are very similar in structural arrangement. The chemical formula of rutin is $C_{27}H_{30}O_{16} \cdot 3H_2O$. Hesperidin has been shown by Szent-Györgyi and others[1] to have a beneficial effect on abnormally fragile capillaries, at least in certain cases. It seemed possible that rutin might have a similar effect. So far as we know, no studies have been reported previously in which rutin has been given to man.

Rutin is a constituent of a variety of plants, including tobacco, garden rue, forsythia, elder flowers, and violets. That used in this study was extracted from tobacco by essentially the same process described by Sando and Lloyd.[2] It had the proper melting point, and its purity and identity were confirmed by carbon and hydrogen determinations and hydrolysis by sulfuric acid to quercetin, dextrose, and rhamnose. The tobacco used was of the flue-cured type, of high quality, cured but not aged or fermented. Lower grades of flue-cured tobacco, the stems of flue-cured tobacco, and air-cured tobacco of any grade, were found to yield little or no rutin.

Rutin was given to 14 patients with hypertension who were attending the cardiac clinic of this hospital. The patients were chosen because they showed an increased capillary fragility, as measured by the Petechial Index of Gothlin.[3] The substance was given by

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1 Armentáno, L., Bensáth, A., Béres, T., Rusznyák, I., and Szent-Györgyi, A., *Deutsche med. Wchnschr.*, 1936, **62**, 1325.

2 Sando, C. E., and Lloyd, J. U., *J. Biol. Chem.*, 1924, **58**, 737.

3 Ahlborg, N. G., and Brante, G., *Act. Med. Scandin.*, 1940, **104**, 527.

mouth in capsules, starting with 20 mg twice a day and, usually, increasing to 3 times a day in a few weeks. Measurement of the Gothlin Index was repeated every 3 or 4 weeks, not oftener, because Gothlin had pointed out that a negative test is only significant if an interval of at least 3 weeks had elapsed since the previous test. Two of the 14 subjects were receiving potassium thiocyanate by mouth at the time the study was begun, and this was continued.

Results. In no case did any toxic effect develop that could be attributed to the rutin. One patient died of a stroke 2 weeks after beginning the medication. Two other patients did not return for adequate follow-up. However, 11 patients were followed for a period varying between 12 and 16 months. Capillary fragility became normal in 8 of these within 2 months of beginning medication, while in 3 it remained increased. One of the subjects in whom the fragility remained high developed a hemiplegia 4 months after beginning medication, and is reported to have died. No complication developed during the period of observation in the remaining 10 subjects, nor was there any significant change in blood pressure. Two subjects stopped taking the rutin after the capillary fragility had returned to normal. Within 6 weeks the capillary fragility was again increased. Rutin was resumed, and when the capillary fragility was tested a month later, it was again normal.

Conclusion. At least in certain cases, rutin appears to have the property of decreasing capillary fragility in subjects in whom this fragility is initially increased. In this effect it resembles hesperidin.